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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/957,709	10/24/1997	HOLLY HOGREFE	1486/41363CP	2438

7590 10/08/2002

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/957,709	HOGREFE ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,16,17,24-27,40-44 and 46-97* is/are pending in the application.

4a) Of the above claim(s) *24-27,40-44,47-58,67-76,81-84,86,93 and 94* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,16,17,46,59-66,77-80,85,87-92 and 95-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 9, 16-17, 24-27, 40-44, 46-97 are pending.

Applicant's amendment of claims 9, 17, 59, 85, 95-96 and cancellation of claims 19-22 in Paper No. 27, filed on 7/29//2002 are acknowledged.

Claims 24-27, 40-44, 47-58, 67-76, 81-84, 86, 93-94 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 08/822774 filed on 3/21/1997.

Drawings

2. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review. Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDOMENT of the application. In addition, if amendments to the specification are needed due to drawing corrections, Applicant is requested to submit

such amendments while the case is being prosecuted to expedite the processing of the application.

Claim Objections

3. Claim 9 and 17 are objected to because the group recited in the claim is written in the alternative form. It is suggested that the term "and" should replace "or" after the last semicolon separating the members of the group. Appropriate correction is required.

4. Claim 46 is objected to because the recitation of "one of" is redundant. It is suggested that the term "one of" be deleted. Appropriate correction is required.

5. Claims 59-66, 77-80, 85, 90 are objected to for the recitation of "P45" or "PEF". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

6. Claim 64 is objected to because it depends on non-elected claim 58. For examination purposes only, the limitations of claim 58 will be considered in the interpretation of the instant claim.

7. Claim 85 is objected to for the recitation of "comprising one or more of SEQ ID NO: 72-73". For clarity, it is suggested that the term "the polypeptides" be inserted between "of" and " SEQ ID NO: ". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 9, 16-17, 95-96 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 9 is indefinite in the recitation of the term "polymerase-enhancing protein complex of one or more wholly or partially synthetic proteins having the same amino acid sequence as the naturally-occurring protein" and the term "polymerase-enhancing protein complex comprising one or more of the naturally occurring or wholly or partially synthetic proteins" for the following reasons. First, the terms are unclear and confusing since there is no antecedent basis for the naturally-occurring protein, therefore one cannot establish which naturally occurring protein is being referred to. In addition, since the wholly or partially synthetic proteins of the first term must have the amino acid sequence of the naturally occurring protein, one cannot establish which wholly or partially synthetic proteins are being recited. In regard to the second term, there is also no antecedent basis for the wholly or partially synthetic proteins therefore one cannot establish which proteins are being referred to or their function. For examination purposes only, the Examiner will assume that the "naturally-occurring, wholly or partially synthetic protein" is any protein of any function. Correction is required.

11. Claims 17 and 96 are indefinite in the recitation of "within about 20 amino acids from the amino terminal end of the protein" as it is unclear and confusing. The term "about" can be interpreted as "more than" or "less than", therefore one cannot clearly establish which location in the protein is being referred to. For examination purposes, the

term "within about 20 amino acids from..." will be interpreted as "20 amino acids from the amino...". Correction is required.

12. Claims 17, 95 and 96 are indefinite in the recitation of "sequence that hybridizes to the complement of the nucleotide sequence" as it is unclear how a sequence can hybridize another sequence. As known in the art, hybridization takes places between nucleic acid molecules and not between sequences. Sequences are graphical representations of how amino acid residues are arranged in a protein. Correction is required.

13. Claim 17 is indefinite in the recitation of "stringent conditions" as it is unclear absent a statement defining the conditions under which the hybridization/wash reaction takes place. Nucleic acids which hybridize under some conditions may not hybridize under different conditions. It is suggested that the experimental conditions of the hybridization/wash reaction be included in the claim. For examination purposes, the term "stringent conditions" will be interpreted as "any conditions". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 9, 16, 17, 63-66, 77-80, 87-92, and 97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

16. Claim 9 is directed to a protein complex having polymerase enhancing activity wherein the complex can have (1) a genus of proteins of any function having a molecular weight of 17-18 KDa and (2) genera of naturally occurring, wholly or partially synthetic proteins of any function and analogs thereof. Claim 16 adds the limitation that the protein complex should have an additional protein of any function from *P. furiosus* having a molecular weight of 17-18 KDa. Claim 17 limits claim 16 by requiring that the protein from *P. furiosus* should comprise (1) the 8 amino acid peptide of SEQ ID NO: 69 or 11 or (2) a polypeptide of any function encoded by a polynucleotide which hybridizes under any conditions to the polynucleotide of SEQ ID NO: 70.

The specification discloses that the polymerase enhancing complex can have the protein of SEQ ID NO: 71 from *P. furiosus*, which under denaturing conditions would have a molecular weight of 17-18 KDa, and that the protein of SEQ ID NO: 71, based on sequence homology, appears to be a dCTP deaminase (page 40, last two paragraphs). The specification also discloses the protein of SEQ ID NO: 19 from *P. furiosus* and based on sequence homology, it appears to be a DFP flavoprotein (page 33-34). While the specification discloses two proteins, their structure and possible function as members of a protein complex having polymerase enhancing activity, no disclosure of the function or structure of other naturally occurring, wholly or partially synthetic proteins or analogs thereof has been provided. In addition, no disclosure of other 17-18 KDa proteins or their function has been provided with the exception of the protein of SEQ ID NO: 71. Furthermore, there is no disclosure of the function of a polypeptide comprising the peptides of SEQ ID NO: 11 or 69, or a polypeptide encoded by a polynucleotide which hybridizes under any conditions to the polynucleotide of SEQ ID NO: 70. No

information as to the critical structural elements a polypeptide should have to display polymerase enhancing activity has been provided either.

While one can argue that some of polypeptides encompassed by the claims can be isolated by sequence comparison using the polypeptides/polynucleotides disclosed in the instant application, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:348-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to be hydroxylases once tested for activity. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification only discloses a single species of the claimed genera which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the claimed genera. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

17. Claim 63 is directed to genera of antibodies which can bind a protein complex comprising the polypeptide of SEQ ID NO: 71. While the specification discloses the polypeptide of SEQ ID NO: 71, many other proteins of unknown function and structure which are part of the claimed protein complex have not been disclosed. An antibody

which binds to any of the unknown proteins of the complex would be encompassed by the claim. Therefore, many antibodies which bind to unknown antigens have not been described. The specification only discloses one species of the claimed genera which is insufficient to put one of ordinary skill in the art in possession of the claimed genera. Thus, one skill in the art cannot conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

18. Claims 64-66, 77-80 are directed to a genus of proteins having a molecular weight of 45 KDa (P45), fusion proteins comprising said genus of P45 proteins, compositions comprising a genus of P45 proteins and compositions comprising analogs of a genus of P45 protein. The specification discloses P45 and P50 as proteins having an apparent molecular weight of 45 and 50 KDa, respectively (page 6, lines 15-16). While the specification discloses one P45 and one P50 protein from *P. furiosus* having the sequence set forth in SEQ ID NO: 71 and 19, respectively, there is no disclosure of the structure or function of other proteins having a molecular weight of 45 (P45) or 50 KDa (P50) from *P. furiosus* or other organisms. There is no disclosure of the critical structural elements a polypeptide of 45 KDa or 50 KDa should have to display polymerase enhancing activity either. As indicated above, while an argument can be made that other P45 or P50 proteins can be isolated by sequence homology, the state of the art clearly teaches the unpredictability of assigning function based on sequence homology. See the teachings of Bork (Genome Research, 10:348-400, 2000), Broun et al. (Science 282:1315-1317, 1998) and Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) already discussed. There is only one P45 and one P50 disclosed, which is insufficient to put one of skill in the art in possession of the claimed genera. Thus, one skill in the art cannot conclude

that Applicant had possession of the claimed invention at the time the instant application was filed.

19. Claims 87-92 and 97 are drawn to a protein extract comprising purified proteins from *Thermus thermophilis* that has dUTPase activity. While the specification discloses the *P. furiosus* polypeptides of SEQ ID NO: 19 and 71 as proteins having polymerase enhancing activity and predicts the function of such polypeptides as being that of a DFP flavoprotein (page 33-34) and a dCTP deaminase (page 40, last two paragraphs), there is no disclosure of proteins from *Thermus thermophilis* which have dUTPase activity. The specification indicates that by sequence homology, one can isolate proteins similar to the *P. furiosus* polypeptides of SEQ ID NO: 19 and 71 in many organisms including *T. thermophilis* (page 44, lines 18-26). However, there is no disclosure of the critical structural elements a homolog of the polypeptide of SEQ ID NO: 19 or 71 should have to display dUTPase activity. As indicated above, the state of the art clearly teaches the unpredictability of assigning function based on sequence homology. See the teachings of Broun et al. (Science 282:1315-1317, 1998), Bork (Genome Research, 10:348-400, 2000) and Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) already discussed. The specification fails to provide adequate description of the claimed invention. Thus, one skill in the art cannot conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

20. Claims 9, 16-17, 85 and 96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 19 and 71, does not reasonably provide enablement for a protein complex comprising any

protein having a molecular weight of 17-18 KDa in denatured form, any protein from *P. furiosus* having a molecular weight of 17-18 KDa in denatured form, any protein from *P. furiosus* comprising the peptides of SEQ ID NO: 69 or 11, any protein encoded by a polynucleotide which hybridizes under any condition to the polynucleotide of SEQ ID NO: 70, any protein comprising the peptides of SEQ ID NO: 72 and 73, any protein encoded by a polynucleotide which hybridizes to a polynucleotide encoding a polypeptide comprising the peptides of SEQ ID NO: 69 or 11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims is not commensurate with the enablement provided in regard to the large number of unknown proteins encompassed by the claims. Claim 9 is drawn to a protein complex having polymerase enhancing activity wherein the complex can have any protein of any function having a molecular weight of 17-18 KDa and any naturally occurring, wholly or partially synthetic proteins of any function and analogs thereof. Claim 16 adds the limitation that the protein complex should have an additional protein of any function from *P. furiosus* having a molecular weight of 17-18 KDa. Claim 17 limits claim 16 by requiring that the protein from *P. furiosus* should comprise (1) the 8

amino acid peptide of SEQ ID NO: 69 or 11 or (2) a polypeptide of any function encoded by a polynucleotide which hybridizes under any conditions to the polynucleotide of SEQ ID NO: 70. Claim 85 is directed to a protein having polymerase enhancing activity comprising one or both of the peptides of SEQ ID NO: 72-73. Claim 96 is drawn to a polypeptide having polymerase enhancing activity encoded by a polynucleotide which hybridizes to a polynucleotide which encodes a polypeptide comprising the peptide of SEQ ID NO: 69 or 11.

As discussed above, while the specification discloses two proteins (SEQ ID NO: 19 and 71), their structure and possible function as members of a protein complex having polymerase enhancing activity, no disclosure of the function or structure of other naturally occurring, wholly or partially synthetic proteins or analogs thereof has been provided. In addition, no disclosure of other 17-18 KDa proteins or their function has been provided with the exception of the protein of SEQ ID NO: 71 (denatured form). Furthermore, there is no disclosure of the function of a polypeptide comprising the peptides of SEQ ID NO: 11 or 69, or a polypeptide encoded by a polynucleotide which hybridizes under any conditions to the polynucleotide of SEQ ID NO: 70. There is no information as to the critical structural elements a polypeptide should have to display polymerase enhancing activity or if the peptides of SEQ ID NO: 11, 69, 72 or 73 are indicative of polymerase enhancing activity.

As indicated previously, while one could argue that some of the polypeptides recited in the claims can be isolated by sequence homology, the current state of the art indicates that small amino acid changes can drastically change the function of a polypeptide. See, for example, the teachings of Van de Loo et al. (Proc. Natl. Acad. Sci.

92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998), already discussed. The amino acid sequence of the polypeptide determines its structural and functional properties, therefore, one of skill in the art would require some knowledge and guidance as to how structure is related to function in order to isolate polypeptides having polymerase enhancing activity. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) screen and isolate those polypeptides of unknown structure and their analogs or (2) determine the function of polypeptides comprising the peptides of SEQ ID NO: 11, 69, 72 or 73, as encompassed by the claims. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

21. Claim 63 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody against the polypeptides of SEQ ID NO: 19 or 71, does not reasonably provide enablement for any antibody which can bind to a polymerase enhancing complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claim is not commensurate with the enablement provided in regard to the large number of unknown antibodies encompassed by the claim. Claim 63

is directed to any antibody which can bind a protein complex comprising the polypeptide of SEQ ID NO: 71. While the specification discloses the polypeptide of SEQ ID NO: 71, many other proteins of unknown function and structure which are part of the claimed protein complex have not been disclosed. An antibody which binds to any of the unknown proteins of the complex would be encompassed by the claim. Therefore, one of skill in the art would have to go through the burden of undue experimentation in order to raise antibodies without the structure of the corresponding antigen. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

22. Claims 64-66 and 77-80 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the P45 protein of SEQ ID NO: 71, does not reasonably provide enablement for any protein having a molecular weight of 45 KDa (P45) or analogs thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided in regard to the large number of unknown proteins having a molecular weight of 45 KDa. Claims 64-66 and 77-80 are drawn to any protein having a molecular weight of 45 KDa (P45), fusion proteins comprising said P45 proteins, compositions comprising any P45 protein and compositions comprising analogs of any P45 protein. The specification discloses P45 and P50 as proteins having an apparent molecular weight of 45 and 50 KDa, respectively (page 6, lines 15-16). While the specification discloses one P45 and

one P50 protein from *P. furiosus* having the sequence set forth in SEQ ID NO: 71 and 19, respectively, there is no disclosure of the structure or function of other proteins having a molecular weight of 45 (P45) or 50 KDa (P50) from *P. furiosus* or other organisms. Even if one assumes that a P45 protein must have polymerase enhancing activity, there is no disclosure of the critical structural elements a polypeptide of 45 KDa or 50 KDa should have to display polymerase enhancing activity either. As indicated above, while an argument can be made that other P45 or P50 proteins can be isolated by sequence homology, the state of the art clearly teaches the unpredictability of assigning function based on sequence homology. The amino acid sequence of a polypeptide determines its structural and functional properties, therefore, one of skill in the art would require some knowledge and guidance as to how structure is related to function in order to determine (1) either the function of any polypeptide of 45 KDa or (2) which polypeptides of 45 KDa have polymerase enhancing activity. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polypeptides, as encompassed by the claims. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

23. Claims 87-92 and 97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the *P. furiosus* polypeptides of SEQ ID NO:

19 and 71, does not reasonably provide enablement for a protein extract from Thermus thermophilis having dUTPase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 87-92 and 97 are directed to any protein or protein extract from *T. thermophilis* with dUTPase activity. The breadth of the claims is not commensurate with the enablement provided by the disclosure with regard to the unknown proteins from *T. thermophilis* with dUTPase activity encompassed by the claim. The specification discloses the *P. furiosus* polypeptides of SEQ ID NO: 19 and 71 as proteins having polymerase enhancing activity and predicts the function of such polypeptides as being that of a DFP flavoprotein (page 33-34) and a dCTP deaminase (page 40, last two paragraphs). The specification also indicates that one of skill in the art can identify similar proteins in many organisms including *T. thermophilis* (page 44, lines 18-26) by sequence homology. The specification does not provide any guidance or examples of *T. thermophilis* dUTPases. No information has been provided on the critical structural elements required to identify a protein with dUTPase activity such as catalytic domain, binding domain, etc. in *T. thermophilis* either. There is no disclosure of the critical structural elements a homolog of the polypeptide of SEQ ID NO: 19 or 71 should have to display dUTPase activity.

The current state of the art teaches that small amino acid changes can drastically change the function of a polypeptide and that sequence identity alone is insufficient to accurately predict function (see the teachings of Broun et al., Van de Loo et al.). Therefore, due to the lack of relevant examples, the amount of information provided, the

lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate *T. thermophilis* proteins with the desired activity. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

24. A 35 USC 112 first paragraph scope of enablement rejection was applied to claims 9, 16, 64, 80 and 87-92 in Paper No. 25, mailed on 2/27/2002.

25. It is noted that new 35 USC 112 first paragraph grounds of rejection have been applied to claims 9, 16, 17, 63-66, 77-80, 85, 87-92, 96-97 in this Office Action.

26. In regard to claims 9, 16 and 80, Applicants argue that it would not require undue experimentation to determine which analogs of P45 have polymerase enhancing activity or which *P. furiosus* proteins would have polymerase enhancing activity since the specification discloses a screening assay in Example 1. In regard to claim 64, Applicants further argue that fusion proteins are well known in the art therefore it would not be undue experimentation to test the claimed fusion proteins using the screening assay of Example 1. In regard to claims 87-92, Applicants argue that the specification does not need to have a working example if the invention is disclosed in a manner that one of skill in the art could practice the invention without undue experimentation. Since the specification discloses a screening assay in Example 1, Applicants conclude that it would

not be undue experimentation to determine if a T. thermophilis protein extract has dUTPase activity.

27. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is agreed that testing for polymerase enhancing activity can be performed with an assay, one would have to first isolate the polypeptides, analogs or protein extracts as encompassed by the claims to test for polymerase enhancing activity. Isolation of such polypeptides, analogs or protein extracts is not routine in the art for the reasons explained above. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

28. Claim 85 was rejected under 35 U.S.C. 102(a) as being anticipated by Bult et al. (PIR accession number F64353, September 16, 1996) and Bult et al. (PIR accession number E64437, September 13, 1996).

29. Claim 85 is rejected under 35 U.S.C. 102(b) as being anticipated by Kletzin (Swiss-Prot accession number Q02103, April 1, 1993), Wang et al. (Swiss-Prot accession number P28248, December 1, 1992), Lundberg et al. (Swiss-Prot accession number P06968, April 1, 1988), Gadsden et al. (Swiss Prot accession number P33317, February 1, 1994), Mercer et al. (Swiss-Prot accession number P14597, April 1, 1990), and Albrecht et al. (Swiss-Prot accession number Q01034, April 1, 1993).

30. These rejections are hereby withdrawn in view of Applicant's amendment of claim 85.

Double Patenting

31. Claims 9, 16-17, 46, 59-66, 77-80, 85, 87-92, 95-97 were rejected under the judicially created doctrine of double patenting over claims 1, 5-9, 13-20, 23-24, 26-34 and 40-41 of US Patent No. 6,183,997.

32. Applicants have indicated that if the instant claims are found allowable, a terminal disclaimer will be filed. Since a terminal disclaimer has not yet been filed and no arguments have been presented pointing out disagreements with the Examiner's contentions, the double patenting rejection is maintained for the reasons of record.

Allowable Subject Matter

33. Claims 46, 59-62 and 95 appear to be allowable over the prior art of record.

34. Claims 46, 59 and 95 would be allowable if rewritten or amended to overcome the objections, double patenting rejection(s), and rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

35. Claims 60-62 would be allowable if rewritten to overcome the objections, double patenting rejection(s), and rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

36. No claim is in condition for allowance.

37. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

38. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
October 1, 2002

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600